

# Prevention of pin tract infection with iodine-supported titanium pins

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## **Prevention of pin tract infection with iodine-supported titanium pin**

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## **Abstract**

*Background* Pin tract infection is one of the most common complications of external fixation. We developed techniques to coat titanium implant surfaces with iodine. This study clinically evaluated infection preventive effects and biological safety of iodine-coated external fixation pins.

*Patients and methods* Iodine-supported pins were placed in 39 limbs of 38 patients. The mean age of the patients was 33.6 years. Twenty-six patients were men and 12 were women. In all patients, the iodine-coated pins were used to prevent infection. There were 476 pin insertion sites. Pin sites were classified according to the Checketts-Otterburns classification (Grade1~6). White blood cells (WBC) and C-reactive protein (CRP) were measured pre- and post-operatively in all patients. To confirm whether iodine from the implant affected physiological functions, thyroid hormone levels in the blood were examined. The change over time for the amount of iodine deposited in the body was calculated from the removed pins.

*Results* External fixation was used for a mean duration of 6 months. Grade 1 infection was found in 2.5% of patients, and grade 2 infection in 1.1%. There was no patient with infection of grade 3 or higher. Median WBC levels were in the normal range and median CRP levels returned to <0.3 mg/dl within 3 weeks after surgery. Abnormalities of thyroid gland function were not detected. The amount of iodine was maintained for a long time with approximately 40% remaining after 1 year.

*Conclusions* Iodine-supported titanium pins were able to decrease pin tract infection rate and had no impact on thyroid function. These results suggest that iodine-coated titanium pins are biologically safe and excellent in prevention of pin tract infections.

## **Introduction**

Pin tract infection is one of the most common complications of external fixation. This type of infection has been reported to occur in over 50% of patients after pin insertion [1, 2]. If the infection does not progress beyond superficial infection, it does not become a major problem. If

the infection reaches a deeper area, then the pins can loosen and the condition can worsen to osteomyelitis. Therefore, prevention of infection is important.

There have been reports on various efforts to reduce the incidence of implant-associated infection. Such efforts included the development of antibacterial pins made of titanium-copper alloys [3] and metal surface treatment involving silver, antibacterial agents, hyaluronic acid, and albumin [4-8]. We have been creating an oxide film on titanium surfaces by anodization and have been developing techniques to impregnate this multiple porous film with the antiseptic properties of iodine (Fig. 1) [9]. This coating can be applied on various types of titanium implants, and a clinical trial has been ongoing since 2008 [10].

In this study, clinical evaluation was performed on the effectiveness and safety of titanium external fixation pins coated with iodine (Fig. 2).

## **Patients and Methods**

This prospective cohort study was approved by the institutional review boards at our institution. The subjects were 38 patients who had undergone external fixation using iodine-coated titanium pins. Informed consent was obtained from patients and family members. The pins were placed in 39 lower limbs. The patients were 26 men (26 limbs) and 12 women (13 limbs). The mean age of the patients was 33.6 years (range, 5-64 years). The diagnoses included 20 cases of limb deformity and shortening, 8 cases of pseudoarthrosis (4 cases of congenital pseudoarthrosis of the tibia [CPT]), 6 cases of fracture, 3 cases of equinus foot, and 2 cases of tumor. The operative procedure was gradual deformity correction in 17 limbs, fixation for fracture or pseudoarthrosis in 13, limb lengthening in 5 and bone transport in 4. There were 476 pin insertion sites: 46 sites in the femur, 335 sites in the lower leg, and 95 sites in the foot. Pin site care consisted of only daily showers.

The infection was evaluated using the Checketts- Otterburn classification [11]. The severity was classified into grades 1 to 6 based on erythema, pain, discharge, and plain x-ray findings (Table

1). Grades 1-3 were superficial infection and grades 4-6 were deep infection. In addition, serum white blood cells (WBC) and C-reactive protein (CRP) were measured before surgery and periodically after surgery.

The biological safety of iodine was evaluated by measuring serum thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4).

Measurements were made to examine the changes over time in the amount of iodine remaining on pins (amount of impregnated iodine). These measurements were made on pins removed from 28 patients (116 pins) when the treatment goals were reached.

#### Statistical analysis

The differences of pin tract infection rate by operative procedure were analyzed by use of the chi-square test, with  $P < 0.05$  for the difference in values considered as being significant.

### Results

External fixation was used for a mean duration of 6 months, and all patients achieved their treatment goals. Twelve patients (12 limbs, 17 sites) had pin tract infection. The infection rate was 3.6% (17/476 sites), and all patients had superficial infection. Infection did not go beyond grade 1 in 8 limbs of 8 patients (12 sites) (2.5%). Infection was grade 2 in 4 limbs of 4 patients (5 sites) (1.1%). There was no patient with infection of grade 3 or higher. The mean time at which infection occurred was 7.2 weeks (range, 3~12 weeks). Two of the 12 patients had reinfection of the pin tract. All cases of infection were resolved by treatment with oral antibiotics alone. No patient had loose or broken pins. The operative procedures in which pin tract infections occurred were 5 deformity corrections (7 sites), 4 fixations (6 sites), 2 bone transport (3 sites) and 1 limb lengthening (1 site) procedures. There was infection in 4.4% of the thigh pin insertion sites (2/46) and 4.5% of the leg pin insertion sites (15/335).

The WBCs at 1, 2, 3, 4, 6, 8, and 12 weeks and 6 months after surgery were:  $7,230 \pm 920/\mu\text{l}$ ,  $6,970 \pm 750/\mu\text{l}$ ,  $6,720 \pm 570/\mu\text{l}$ ,  $5,790 \pm 370/\mu\text{l}$ ,  $5,830 \pm 280/\mu\text{l}$ ,  $6,320 \pm 480/\mu\text{l}$ ,  $6,680 \pm 450/\mu\text{l}$ , and  $6,230 \pm 660/\mu\text{l}$ , respectively. All values were under  $8,000/\mu\text{l}$ . The CRP levels were  $1.99 \pm 0.62$  mg/dl,  $0.89 \pm 0.34$  mg/dl,  $0.33 \pm 0.13$  mg/dl,  $0.42 \pm 0.17$  mg/dl,  $0.33 \pm 0.10$  mg/dl,  $0.47 \pm 0.16$  mg/dl,  $0.42 \pm 0.18$  mg/dl, and  $0.11 \pm 0.03$  mg/dl, respectively. The values for all patients normalized to 0.5 mg/dl or less within 3 weeks after surgery.

The levels of thyroid hormones TSH, FT3, and FT4 were  $1.81 \pm 0.28$   $\mu\text{IU/ml}$ ,  $2.76 \pm 0.14$  pg/ml, and  $1.27 \pm 0.06$  ng/dl, respectively, at 2 weeks after surgery;  $1.92 \pm 0.23$   $\mu\text{IU/ml}$ ,  $2.85 \pm 0.11$  pg/ml, and  $1.22 \pm 0.06$  ng/dl at 4 weeks after surgery;  $1.93 \pm 0.26$   $\mu\text{IU/ml}$ ,  $2.81 \pm 0.13$  pg/ml, and  $1.15 \pm 0.06$  ng/dl at 8 weeks after surgery;  $1.90 \pm 0.31$   $\mu\text{IU/ml}$ ,  $3.08 \pm 0.13$  pg/ml, and  $1.24 \pm 0.05$  ng/dl at 12 weeks after surgery; and  $1.98 \pm 0.52$   $\mu\text{IU/ml}$ ,  $2.93 \pm 0.11$  pg/ml, and  $1.26 \pm 0.04$  ng/dl at 6 months after surgery. There was no patient with abnormal values.

In the removed pins, the mean percentages of iodine remaining were 41.6% of the original amount at 0-4 months, 49.8% at 5-8 months, and 42.0% at 9-12 months (Table 2).

## Discussion

In external fixation, it has been previously reported that infection occurs in 50% or more of the pin insertion sites when no preventive measures are taken [1, 2]. In our study, pin tract infection occurred in 12 limbs of 12 patients, 3.6% of the pin insertion sites (17/476 sites). Iodine-supported titanium pins may reduce the rate of pin tract infection.

All patients in our study had superficial infection of severity grades 1-2. In previous reports, superficial infection was seen in much higher percentages of patients at 16-74.1% [12-14]. In our patients, WBC was normal and CRP normalized 3 weeks after surgery. Thus, hematological findings also showed that iodine-coated pins had a high ability to control infection at the insertion sites (Fig. 3). Lee et al. [15] reported that pin tract infection rate could be reduced using polyhexamethylene biguanide-impregnated gauze. If iodine-supported pins are used together with

polyhexamethylene biguanide-impregnated gauze, the infection rate may be further reduced. Iodine-coated pins prevent not only surface infection, but also deep infection, because the antimicrobial coating with iodine covers the whole pin.

Basic research has been conducted regarding various metal surface treatments to reduce the rate of implant-associated infection [3-8]. Masse et al. [16] used silver-coated pins for external fixation and reported an infection rate of 30%. Other studies have reported on silver-coated pins for external fixation [17, 18]. However, some studies have raised concerns over clinical toxicity of silver coating [15, 19].

For an antibacterial coating, Popat et al. [20] fabricated nanotubes on titanium surfaces by oxidation. They reported on the techniques, including loading the nanotubes with the antibiotic gentamicin. Another report described prevention of pin tract infection by fitting gentamicin-coated sleeves over the pins [21]. These studies were basic research and not clinical trials. Antibacterial agents have disadvantages. The development of resistant bacteria is unavoidable, and the effectiveness of these agents will not last long term.

Since 2005, we have been developing techniques to treat titanium surfaces with iodine using a special method [9]. Iodine has been used widely in clinical practice as an antiseptic and contrast medium. It is a substance whose safety has been confirmed. In addition, iodine has a broad antimicrobial spectrum against common bacteria, fungi, and common viruses. Another advantage is that it does not cause resistant bacteria.

The relationship between operative procedure and pin tract infection was investigated. In patients with superficial infection of pin site, the operative procedure was deformity correction in 5 patients (7 sites), fixation in 4 patients (6 sites), bone transport in 2 patients (3 sites), and limb lengthening in 1 patient (1 site). Thus, infection rate was 3.3% (7/215 sites) in deformity correction, 4.0% (6/149 sites) in fixation, 7.0% (3/43 sites) in bone transport and 1.5% (1/69 sites) in limb lengthening. There were no obvious differences by operative procedure ( $P=0.47$ ).

Additional factors that may contribute to pin tract infection include the thickness of the soft tissue mantle between the skin and bone, with anatomical areas with thicker soft tissue envelopes, such as the thigh, associated with higher infection rates [22]. In our study, there were 17 sites with superficial infection, of which 2 sites were in the femur (4.4% of the femoral pin insertion sites) and 15 sites were in the lower leg (4.5% of the lower leg pin insertion sites). Thus, there was no difference in the infection rates by site. These results indicate that iodine coating does not affect the infection rate, which is influenced by the amount of soft tissue at the pin insertion. This may be due to the antimicrobial efficacy of iodine coating.

Our study examined the safety of iodine-coated pins. There was no patient with abnormal thyroid hormone levels after surgery. Iodine is an essential trace element in the human body and exists in our body in thyroid hormones. It is thought to have low toxicity in the body.

In our study, no loosening around the pins was observed radiographically during treatment. Thus, it was determined that there was no local toxicity of iodine.

Our study also examined the duration of the sustained effect by measuring the amount of remaining iodine in the removed pins. The mean percentage of remaining iodine was  $41.6 \pm 17.3\%$  at 0-4 months,  $49.8 \pm 19.9\%$  at 5-8 months, and  $42.0 \pm 16.7\%$  at 9-12 months. Although the amount of iodine decreased to 40~50% at an early stage comparatively, it was retained for one year. The reason why more iodine remained in patients with the long-term fixation is unclear. However, we speculate that the amount of remaining iodine depends on the environment of the pin sites or individual variability of the patients. Namely, the degree of exudate around pin tracts would affect the release of iodine on the surface. The duration of the sustained effect was better for iodine-coated pins than for antibacterial agents. Thus, our findings suggest that iodine-coated pins are effective in prevention of delayed-onset infection.

Iodine coating might also be applicable to other titanium implants for orthopedic surgery, implants in dental and oral regions, heart valve prostheses, cochlear implants, and catheters.



Iodine-supported pins for external fixation have good biological safety and tissue compatibility. These pins are clinically useful to control infection at a pin insertion site.

**Conflict of interest** The authors declare that they have no conflict of interest.

## References

1. Mahan J, Selgison D, Henry SL, Hynes P, Dobbins J. Factors in pin tract infections. *Ortho*. 1991;14:305-8.
2. Lee-Smith J, Santy J, Davis P, Jester R, Kneale J. Pin site management. Towards a consensus: part I. *J Orthop Nurs*. 2001;5:37-42.
3. Shirai T, Tsuchiya H, Shimizu T, Ohtani K, Zen Y, Tomita K. Prevention of pin tract infection with titanium-copper alloys. *J Biomed Mater Res B Appl Biomater*. 2009;91:373-80.
4. Shi Z, Neoh KG, Kang ET, Wang W. Antibacterial and mechanical properties of bone cement impregnated with chitosan nanoparticles. *Biomaterials*. 2006;27:2440-9.
5. Nohr RS, Macdonald JG. New biomaterials through surface segregation phenomenon: new quaternary ammonium compounds as antibacterial agents. *J Biomater Sci Polym Ed*. 1994;5:607-19.
6. Kinnari TJ, Peltonen LI, Kuusela P, Kivilahti J, Könönen M, Jero J. Bacterial adherence to titanium surface coated with human serum albumin. *Otol Neurotol*. 2005;26:380-4.
7. Ewald A, Glückermann SK, Thull R, Gbureck U. Antimicrobial titanium/silver PVD coatings on titanium. *Biomed Eng Online*. 2006;5:22.
8. Harris LG, Richards RG. Staphylococcus aureus adhesion to different treated titanium surface. *J Mater Sci Mater Med*. 2004;15:311-4.
9. Shirai T, Shimizu T, Ohtani K, Zen Y, Takaya M, Tsuchiya H. Antibacterial iodine-supported titanium implants. *Acta Biomater*. 2011;7:1928-33.

10. Tsuchiya H, Shirai T, Nishida H, Murakami H, Kabata T, Yamamoto N, Watanabe K, Nakase J. Innovative antimicrobial coating of titanium implants with iodine. *J Orthop Sci.* 2012;17:595-604.
11. Checketts RG, MacEachern AG, Otterburn M. Pin track infection and the principles of pin site care. In: De Bastiani A, Graham Apley A, Goldberg A, editors. *Orthofix external fixation in trauma and orthopaedics*. Berlin: Springer; 2000. p. 97-103
12. Ahlborg HG, Josefsson PO. Pin-tract complications in external fixation of fractures of the distal radius. *Acta Orthop Scand.* 1999;70:116-8.
13. Barbarossa V, Matković BR, Vucić N, Bielen M, Gluhinić M. Treatment of osteomyelitis and infected non-union of the femur by a modified Ilizarov technique: follow-up study. *Croat Med J.* 2001;42:634-41.
14. Davies R, Holt N, Nayagam S. The care of pin sites with external fixation. *J Bone Joint Surg Br.* 2005;87:716-9.
15. Lee CK, Chua YP, Saw A. Antimicrobial gauze as a dressing reduces pin site infection: a randomized controlled trial. *Clin Orthop Relat Res.* 2012;470:610-5.
16. Massè A, Bruno A, Bosetti M, Biasibetti A, Cannas M, Gallinaro P. Prevention of pin track infection in external fixation with silver coated pins: clinical and microbiological results. *J Biomed Mater Res.* 2000;53:600-4.
17. Collinge CA, Goll G, Seligson D, Easley KJ. Pin tract infections: silver vs uncoated pins. *Orthopedics.* 1994;17:445-8.
18. Wassall MA, Santin M, Isalberti C, Cannas M, Denyer SP. Adhesion of bacteria to stainless steel and silver-coated orthopedic external fixation pins. *J Biomed Mater Res.* 1997;36:325-30.
19. Kraft CN, Hansis M, Arens S, Menger MD, Vollmar B. Striated muscle microvascular response to silver implants: A comparative in vivo study with titanium and stainless steel. *J Biomed Mater Res.* 2000;49:192-9.

20. Popat KC, Eltgroth M, Latempa TJ, Grimes CA, Desai TA. Decreased Staphylococcus epidermis adhesion and increased osteoblast functionality on antibiotic-loaded titania nanotubes. *Biomaterials*. 2007;28:4880-8.
21. Forster H, Marotta JS, Heseltine K, Milner R, Jani S. Bactericidal activity of antimicrobial coated polyurethane sleeves for external fixation pins. *J Orthop Res*. 2004;22:671-7.
22. Parameswaran AD, Roberts CS, Seligson D, Voor M. Pin tract infection with contemporary external fixation: how much of a problem? *J Orthop Trauma*. 2003;17:503-7.

## Figure Captions

Figure 1 : Electron micrograph of the oxide layer

a, More than 100,000 pores/mm<sup>2</sup>

b, Magnified image

Figure 2 : Iodine-coated pins

Figure 3 : Condition around pins at six months

Table 1: Checketts- Otterburn classification of pin site infections

Table 2: Chronological amount change of coated iodine

Figure 1a

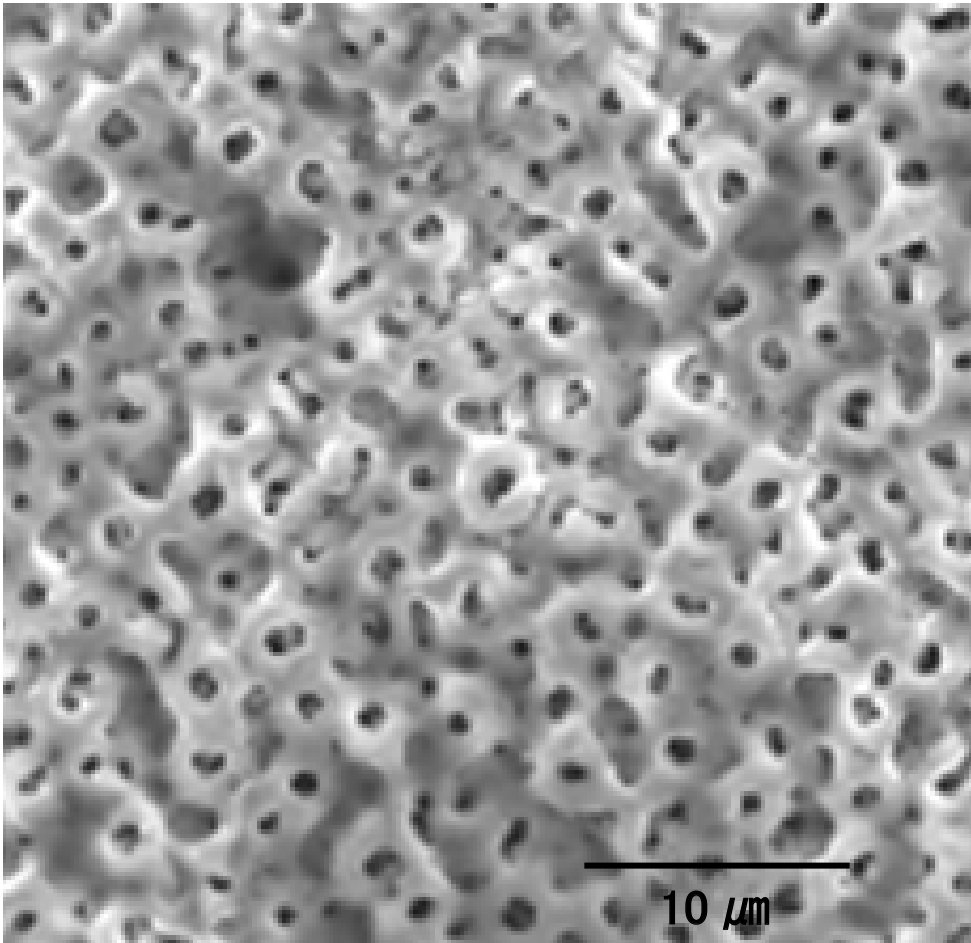


Figure 1b

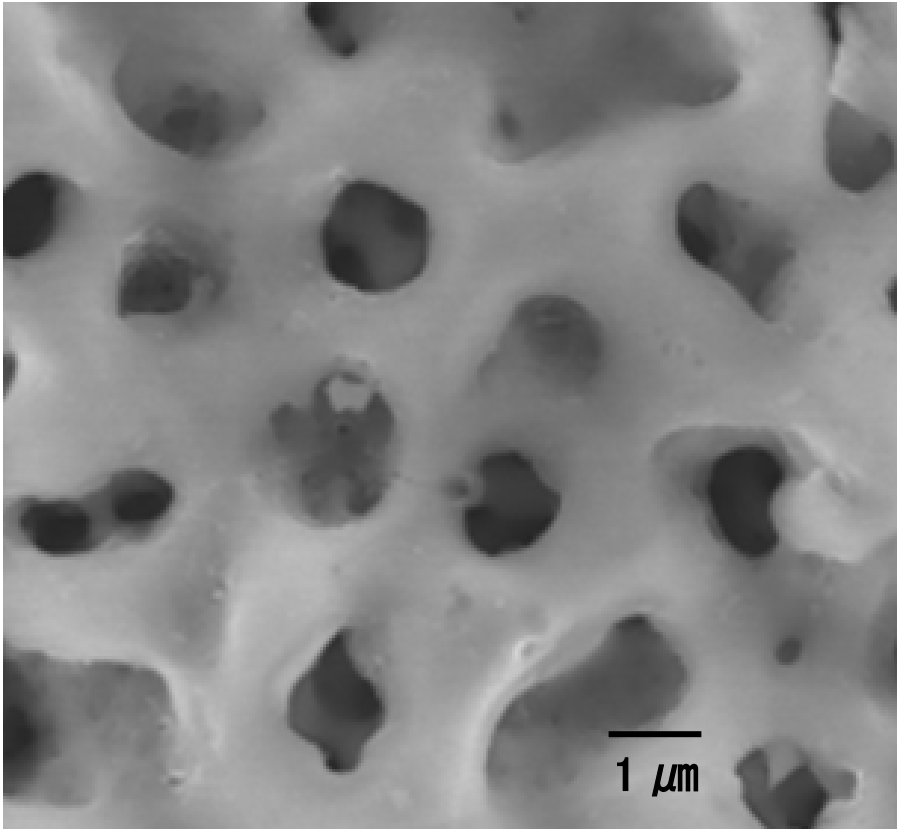


Figure 2

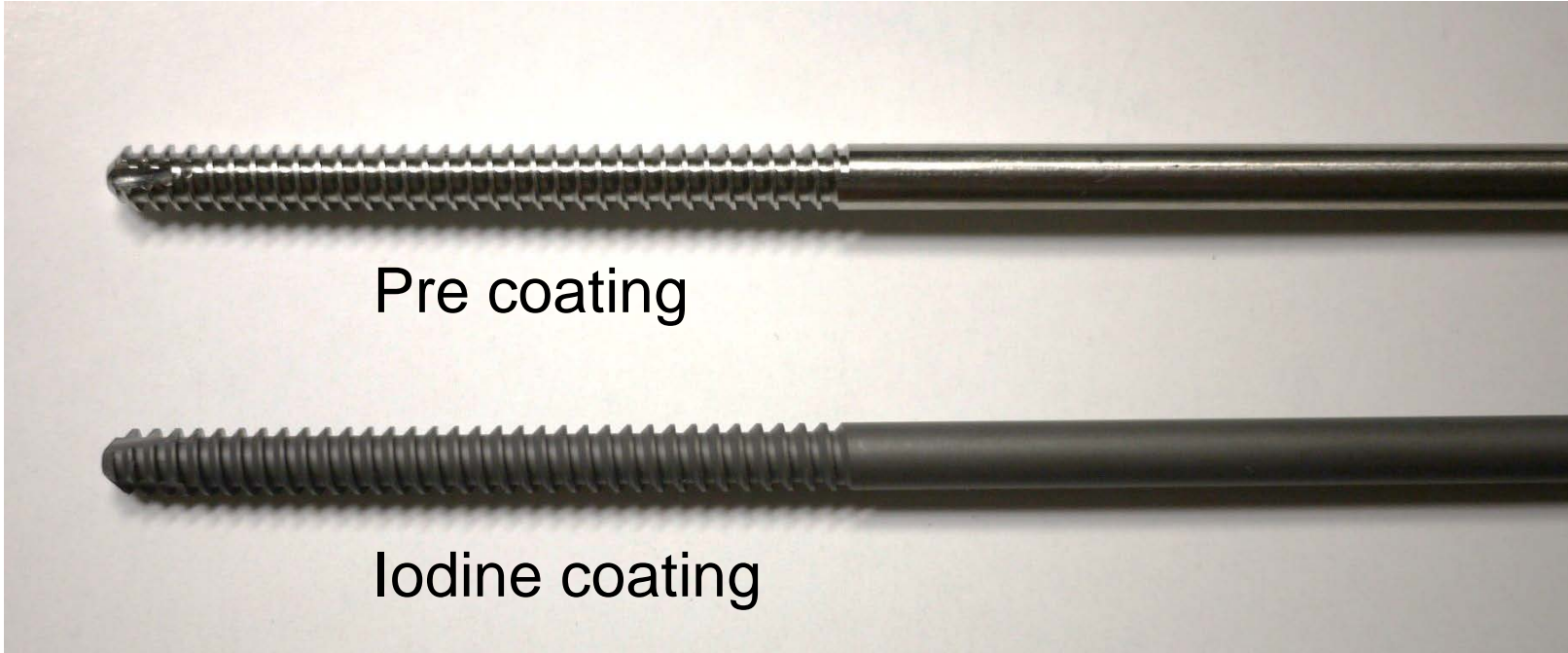


Figure 3

